Results: After a mean f/u of 105 months the rate of LR at 10 years was 12.0%, and the DFR was 70.8% in this young patient set. Age was not a significant cut point for either endpoint. For LR the n-ratio was the first cut point (table A) at 16%, followed by PR status. For DFR there was a dramatically low cut point in n-ratio of 9%, followed by tumor location and T-stage (table B).
Conclusion: We hypothesize that after BCS, ST and RT, subgroups of young patients are at higher risk, determined mostly by the n-ratio, not number of positive nodes. Higher risk is also indicated for medially and centrally located tumors, in PR negative patients and in women presenting with T2 N pos tumors. These subgroups may need a more aggressive therapy. The present results differ from most published reports, where lymph node status is not found critical to the likelihood of local recurrence.

906 ORAL

An interobserver study comparing CT and MRI for GTV delineation in radiotherapy for cervical cancer

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Background: This study evaluated the interobserver and intermodality variation using CT and MR imaging for delineation of gross tumour volume (GTV) in cervical tumours.
Methods: 4 observers (2 radiation oncologists and 2 radiologists) with specialisation in gynaecological oncology outlined the GTV independently on contrast-enhanced CT and MRI scans of 18 patients with cervical cancer. The scans were co-registered and areas of spatial difference between observers and modalities were determined. The volume common to all observers on each scan (V_{com}) and the total encompassed volume (V_{tot}) were measured to assess interobserver variation.
Results: *Intermodality comparison*: The mean tumour volume with CT was 133.9 cm^3 (range 28.2–422.5, SD 119.4) and 73 cm^3 (range 9.4–236 cm^3, SD 74.7) using MRI. The average CT/MRI ratio was 2.5 (SD 1.4), and in all cases the CT volume was larger than with MRI. There was greater interscan variation with smaller tumours, with CT/MRI ratio 3.1 for tumours <50 cm^3 on MRI compared to a ratio of 1.6 for volumes >50 cm^3. The largest discrepancy between modalities was in the superior-inferior directions, with large variation in contours involving the uterine body and vagina. For smaller tumours the entire cervix was often outlined on the CT images due to observer uncertainty.
Interobserver variation: The V_{tot}/V_{com} ratio was 3.3 (SD 1.6) for CT and 3.7 (SD 2.4) for MRI. For all 36 scans, the V_{com} was always smaller than smallest individual observer volume. The interobserver variation was greatest for smaller tumours, with ratio 4.8 for tumours <50 cm^3, and 1.9 for volume >50 cm^3 on MRI, and 4.1 for tumours <100 cm^3 and 2.5 tumours >100 cm^3 on CT. The average ratio between the individual volume and mean tumour volume (and SD), was 0.9 (0.3), 1.0 (0.3), 1.1 (0.2), 1.0 (0.2) for CT, and 0.7 (0.2), 1.2 (0.3), 1.2 (0.3), 0.9 (0.1) for MRI for observers 1, 2, 3 and 4 respectively.
Conclusion: The GTV was on average 250% larger on CT compared to MRI. The MRI scans were particularly useful for defining uterine and vaginal extent of disease. There is large interobserver variation, which has similar magnitude with both CT and MRI, and is greatest with small tumours. This variation should be taken into account when defining GTV, which is increasingly required for planning an integrated boost with IMRT and for 3D brachytherapy.

907 ORAL

Dose escalation with simultaneous integrated boost intensity-modulated radiotherapy for cervical cancer – impact of interfractional organ motion

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Aims: To assess whether the dosimetric advantage of IMRT compared to conformal radiotherapy (CRT) in reducing normal tissue doses is maintained throughout a course of radiotherapy, and that target volume definition is sufficient to account for interfractional movement. In addition, the feasibility of dose escalation with simultaneous integrated boost (SIB-IMRT) to be used in conjunction with intrauterine brachytherapy was evaluated.
Methods: 10 patients with cervical cancer had an RT planning CT scan, and 2 additional scans in the 2nd and 4th weeks of treatment. GTV, CTV and normal structures were outlined on all 30 scans. SIB-IMRT plans were produced to deliver 54, 58 and 60 Gy to PTV1 (GTV+5 mm) and 50.4$_{eq}$ Gy to PTV2 (CTV+15 mm). These were compared to delivering standard dose 50.4 Gy to PTV2 with CRT and IMRT. Treatment fields were applied to subsequent scans, and the impact of organ motion on dose to GTV, CTV and normal tissues were assessed.
Results: On the initial scans, normal tissue receiving >50.4 Gy with CRT, IMRT and SIB-IMRT (60 Gy) respectively were: bladder: 35%, 21%, 30%; rectum: 29%, 24%, 31%; large bowel: 43 cm^3, 12 cm^3, 14 cm^3; small bowel: 138 cm^3, 27 cm^3, 51 cm^3. The mean GTV volume reduced from 68 cm^3 to 59 cm^3, 53 cm^3, and the CTV from 656 cm^3 to 610 cm^3, 576 cm^3 in weeks 2 and 4 respectively. Coverage by 95% isodose of GTV, CTV was: CRT 100%, 99.6% and IMRT 99.9%, 99.5% in week 2; CRT 100%, 99.4% and IMRT 100%, 99.3% in week 4. SIB-IMRT$_{60}$ mean tumour dose was 59.9 Gy, and 93.9% GTV received >57 Gy. Normal tissue doses on repeat scans with CRT, IMRT and IMRT-SIB were: bladder: 33%, 24%, 31%; rectum: 22%, 18%, 26%; large bowel: 77 cm^3, 30 cm^3, 41 cm^3; small bowel: 144 cm^3, 52 cm^3, 64 cm^3 in week 2, and bladder: 36%, 32%, 36%; rectum: 37%, 28%, 35%; large bowel: 79 cm^3, 42 cm^3, 52 cm^3; small bowel: 189 cm^3, 88 cm^3, 99 cm^3 in week 4.
Conclusions: IMRT reduces dose to normal structures by up to 40% on the initial scan. SIB-IMRT can increase the external beam dose to tumour by 20% whilst maintaining normal tissue doses less than with CRT. With interfractional movement, there is increased normal tissue doses with all techniques, but IMRT and SIB-IMRT still irradiate less normal tissue than CRT. The selected CTV-PTV margin is sufficient to ensure adequate dose to GTV and CTV throughout treatment.

Poster presentations (Wed, 26 Sep, 14:00−17:00)
Radiotherapy/radiobiology

908 POSTER

The up-regulation of Integrin Linked Kinase in oral epithelium (mouse) by fractionated irradiation is accelerated by Keratinocyte Growth Factor (Palifermin)

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Background: Early radiation effects in oral mucosa are a severe and often dose-limiting side effect of radiotherapy for advanced head-and-neck tumours. The regeneration response to daily fractionated irradiation, summarized as "repopulation", occurs with a delay of about 1 week after the first fraction, and subsequently results in an increase in mucosal radiation tolerance with increasing overall treatment time. The present study in mouse tongue mucosa was initiated to determine changes in the expression of Integrin Linked Kinase (ILK) during fractionated irradiation, and their modulation by administration of Keratinocyte Growth Factor. ILK links integrins with growth factor receptors and thus modulates intracellular signal transduction. Variations in ILK expression hence may contribute to the regulation of the repopulation processes.
Materials and Methods: Daily fractionated irradiation with 5 X 3 Gylweek was given to the snouts of mice over a total of 2 weeks. In an additional experimental arm, Keratinocyte Growth Factor (Palifermin) was administered as a single injection of 15 mg/kg at the day before the first fraction. Groups of 3 mice per day were sacrificed from day 0 to 16, and the tongues were processed for immunohistochemistry. ILK expression was analysed semi-quantitatively using an arbitrary score for the staining signal.
Results: Compared to un-irradiated controls, an increase in the expression of ILK was found at the end of the first treatment week, i.e. in coincidence with the onset of repopulation. Administration of Palifermin on day −1 resulted in an almost immediate stimulation of ILK expression already on day 0, which remained elevated during the entire first week of irradiation, before a return to control values was observed at the beginning of week 2.
Conclusions: Fractionated irradiation results in a delayed increase in the expression of ILK in oral epithelium, indicating a regulatory role of this protein in the mucosal regeneration response. The earlier stimulation of ILK expression by KGF suggests that this growth factor modulates the intracellular signal transduction via this pathway, eventually resulting in increased mucosal tolerance to fractionated irradiation.
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909 POSTER

Updated results of high dose proton beam therapy (PBT) for stage I non-small cell lung cancer (NSCLC)

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Background: Proton beam has a distinctive depth-dose curve that enables us to deliver higher doses to the tumor without increasing doses to the